REMARKS

Claims 1, 8, 9, 18, 19, 40, 41, 43, and 50-60 were pending. Claim 8 is allowed.

Claims 1, 9, 43, and 60 have been amended in view of the Examiner's comments under 35 U.S.C. §112, first and second paragraphs provided in the Office Action mailed on December 11, 2003 to clarify limitations of the claimed invention. In addition, Applicants have removed the phrase: "of nucleotides 119-1831" from claim 1, where it was inadvertently included in the text of the claim in the response filed on September 16, 2003. It was not intended as an amendment to the claim and was not described as an amendment in the response. Thus, the phrase has been deleted from the listing of pending claims provided herein.

Applicants have submitted a replacement Sequence Listing herewith. The Sequence Listing has been amended to include SEQ ID NOs:45, 46, and 47, which were previously referred to in the specification by their Genbank accession numbers, U89672, AA213817, and W86797, respectively. Claims 1, 9, 43, and 60 have been amended to replace the Genbank accession number with a SEQ ID NO. No new matter has been added.

Rejections Under 35 U.S.C. §112, First Paragraph

The Examiner rejected claims 1, 9, 18, 19, 40, 50-56, 59, and 60 under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. Applicants respectfully traverse the rejection.

The Examiner asserts that the genus of claimed nucleic acids for which "no written description is provided in the specification" and suggests that the genus "comprises hundreds of billions of different possibilities." (Office Action mailed 12/11/2003, page 4). In the rejection of the claims, the Examiner has alleged that the specification does not provide sufficient descriptive information, such as structural information, to meet the written description guidelines [Federal Register: December 21, 1999 (Vol. 64, Number 244), revised guidelines for written description] or the written description requirements set forth in *Regents of the University of California v. Eli Lilly & Co.* 119 F.3d 1559, 43 USPQ 2d 1398 (Fed. Cir. 1997). Applicants respectfully disagree with the Examiner's conclusions for the following reasons.

The basic requirement of the written description requirement is that the claimed invention must be described clearly enough to allow one of ordinary skill in the art to recognize that the

inventors invented the claimed invention. *Vas-Cath v. Mahurkar* 935 F.2d 1555, 19 USPQ2d 1111 (Fed. Cir. 1991); *Lockwood v. American Airlines, Inc.* 107 F.3d 1565, 41 USPQ2d 1961 (Fed. Cir. 1997); *In re Gosteli* 872 F.2d 1008, 10 USPQ 2d 1614 (Fed. Cir. 1989). The requirement is based on the knowledge of the skilled artisan in the particular art: the applicant must convey to one of ordinary skill in the art through the disclosure in the invention that the applicant was in possession of the claimed invention. The *Lilly* case does not prohibit definition of a genus of nucleic acid molecules by hybridization to a reference sequence. *Id.* The *Lilly* case merely states that a DNA molecule must be described by a precise definition, "such as by structure, formula, chemical name or physical properties." *Id.*

The claims rejected by the court in the *Lilly* case differ substantially from the instant claims under consideration. The claims in *Lilly* included a claim to a "nucleotide sequence having the structure of the reverse transcript of an mRNA of a [human], which mRNA encodes insulin". The *Lilly* court stated that the claim required human insulin-encoding cDNA, but concluded that because the application lacked any disclosure of a human cDNA sequence, it lacked adequate written description of such a cDNA. *Id.* In contrast, the claims in the instant application are drawn to (a) nucleic acid molecules that hybridize to DNA sequences that are provided, under stringent hybridization conditions, (b) degenerates of the provided sequences, and complements of (a) and (b). Applicants respectfully assert that the basis for the lack of written description found by the *Lilly* court does not apply in the instant case. Unlike the *Lilly* application, Applicants have provided a written description of the claimed sequences, including specific DNA sequences, specific stringent hybridization conditions, and descriptions of the degenerate features of the genetic code. Thus, Applicants have described the claimed invention in a way that makes clear to one of ordinary skill in the art that Applicants were in possession of the invention at the time of filing.

A genus of nucleic acid molecules is not routinely defined in the art by a listing of sequences, chemical formulas or chemical names. Instead, one of the ways the art routinely identifies nucleic acid molecules is by the ability of the nucleic acid molecules to hybridize to a particular nucleotide sequence. Hybridization conditions in combination with a reference sequence provide a precise definition of the claimed hybridizing nucleic acid molecules by physical properties that satisfy the criteria set forth by the court in the *Lilly* case. *Id.* This sort of

identification describes the physical properties of a genus of nucleic acid molecules as surely as IR and MS spectra describe the physical properties of a set of chemical compounds.

As one of ordinary skill in the art knows, the claimed molecules must be sufficiently like the reference sequence isolated from sarcoma cells to hybridize under the specifically defined set of stringent hybridization conditions. The person of ordinary skill in the art would recognize, in accordance with the standard practice in the art that Applicants' invention includes a limited genus of nucleic acid molecules so closely related by physical structure to SEQ ID NOs: 1, 38, or 43 that hybridization under stringent conditions is possible. The person of skill in the art would recognize that Applicants invented the claimed genus based on the description of the claimed sequences in the specification. Therefore, Applicants have fulfilled the requirement of the law for providing an adequate written description of the claimed invention.

One of ordinary skill in the art can readily identify whether a particular sequence is part of the claimed genus. Thus, because Applicants have provided an adequate written description of the claimed invention, one of ordinary skill in the art will be certain if a particular sequence is, or is not, part of the claimed genus.

SEQ ID NOs:1, 38, and 43 not only are representative of each claimed genus, but in fact are the sequences to which each member of the genus of nucleic acid molecules is related by physical properties (hydrogen bonding of the complementary hybridizing strands of a double-stranded nucleic acid molecule). Each sequence in each genus, therefore, must be closely related in nucleotide sequence to SEQ ID NOs:1, 38, or 43 in order to satisfy the definition of the respective claimed genus.

The Examiner states on page 4 of the Office Action that no written description is provided for variants, which would be included in the claimed genus. Applicants respectfully disagree and assert that variants per se are not claimed but rather the claimed variants include only minor nucleotide changes in the nucleic acids provided. Applicants assert that one of ordinary skill in the art would recognize that a nucleic acid molecule having a single nucleotide difference from SEQ ID NOs:1, 38, or 43 was within the genus described by Applicants and thus Applicants are entitled to claim such nucleic acid molecules. Similarly, nucleic acid molecules having only a few nucleotide differences from the disclosed sequence are recognizable by one of ordinary skill in the art as belonging to the genus of nucleic acid molecules invented by

Applicants. Accordingly, Applicants should be entitled to claim such molecules, having adequately described the genus containing such nucleic acid molecules.

The Examiner appears to indicate at page 4 of the Office Action that Applicants are only entitled to claims encompassing sequences *expressly* included in the application as filed. The Examiner cites *Fiers v. Sugano* and *Amgen v. Chugai* support of the rejection and states that "there is no record or description which would demonstrate conception of any nucleic acids other than those expressly disclosed." Applicants respectfully disagree. Applicants submit that *Fiers v. Sugano* states: "what is required is a **description** of the DNA itself". *Fiers v. Sugano* 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (emphasis added). The Fiers court further stated that one could provide an adequate written description of a nucleic acid "such as by structure, formula, chemical name or physical properties". *Id.* Applicants have done just that in the specification. Applicants have set forth the physical properties of the genus as including nucleic acid molecules that hybridize to SEQ ID NOs:1, 38, or 43, and have also set forth the functional properties of the genus as including nucleic acids that encode a tumor-associated, e.g. a sarcoma-associated, polypeptide. Applicants respectfully assert that those of ordinary skill in the art would fully understand and recognize that Applicants were in possession of the molecules that fall within the claimed genus, including nucleic acid molecules that differ from SEQ ID NO: 1, SEQ ID NO:38 and SEQ ID NO:43 due to the degeneracy of the genetic code.

Applicants respectfully assert that the Written Description requirement does not require that each and every member of a claimed genus of nucleic acids be expressly disclosed in the specification, but rather requires that sufficient description be provided to allow one of ordinary skill to recognize that Applicants were in possession of the claimed invention. Applicants submit that adequate written description to meet this requirement is provided in the specification as filed.

Claims 1 and 60

With regard to claims 1 and 60, the sequences claimed are described as nucleic acid molecules that hybridize to a nucleotide sequence selected from the group consisting of SEQ ID NOs:38 and 43 (for claim 1) or SEQ ID NO:1 (for claim 60) under the specific highly stringent hybridization conditions in the claim and the claimed nucleic acid molecules must also encode a

sarcoma associated gene product. Thus, the number of possible sequences that meet these specific structural and functional criteria are limited and defined. Applicants assert that these express limitations provide to one of ordinary skill in the art "guidance on the identification of the sequences which hybridize to the target sequences" (Office Action at page 5).

With respect to section (b) of claims 1 and 60, the sequences claimed are nucleic acid molecules that differ from the nucleic acid molecules of SEQ ID NOs: 38 and 43 (for claim 1) or SEQ ID NO:1 (for claim 60) in codon sequence due to the degeneracy of the genetic code. Applicants submit that the features of the degeneracy of the genetic code are well known to those of ordinary skill in the art, and further assert that the description of a number of examples of the degeneracy of the genetic code are provide at page 13, lines 15-27, and include specific disclosures of codons that may be substituted in the sequences of the invention due to the degeneracy of the genetic code.

Parts (c) of claims 1 and 60 are drawn to complements of parts (a) and (b), which include molecules that Applicants assert one of ordinary skill would clearly recognize and understand. Applicants submit that the basis for complement identity – Watson-Crick base pairing – has been well known in the art for many years and thus the inclusion of complements in the claimed genus of nucleic acids would be clear to one of ordinary skill

Thus, based on the specific teachings and examples of the claimed nucleic acid sequences of the invention in the specification, one of ordinary skill in the art would recognize that Applicants were in possession of the claimed sequences at the time of filing. Applicants respectfully request withdrawal of the rejection of claims 1 and 60, and claims 18, 19, 50-56, which depend from claim 1, under 35 U.S.C. §112, first paragraph.

Claim 9

The Examiner rejected claim 9 under 35 U.S.C. §112, first paragraph. Applicants respectfully submit that adequate support for the claimed fragments and their complements is provided in the specification as filed. The fragments as claimed include pieces of nucleotides 1-1997 of SEQ ID NO:38 that are between 12 and 1996 nucleotides in length that encode a part of SEQ ID NO:39 that is between 7 and 100 amino acids in length. Similarly, claim 9 also encompasses pieces of nucleotides 1-2442 of SEQ ID NO: 43, between 12 and 2441 nucleotides

in length that encode a part of SEQ ID NO:44 that is between 7 and 100 amino acids in length.

Applicants assert that these limitations in the claim clearly delineate and define the claimed molecules, and that one of ordinary skill in the art would recognize that Applicants were in possession of the claimed invention at the time of filing. Nucleotide sequences SEQ ID NOs:38 and 43 are provided in the application and at page 13, line 28 through page 15, line 16, the application also provides descriptions of fragments and methods with which to determine whether the fragments encoded a part of SEQ ID NO: 39 and 44, respectively. In addition, at page 16, line 19 through page 21, line 13 of the specification, Applicants provide guidance as to how to make polypeptides and fragments of polypeptides and the specification also provides the entire amino acid sequences of polypeptides of the invention, e.g. SEQ ID NOs:39 and 44. Thus, Applicants have described whole sequences and fragments of both DNA and protein and accordingly, one or ordinary skill in the art would know that Applicants were in possession of all claimed fragments at the time of filing.

Applicants submit that one of ordinary skill would easily make and test an array of such nucleic acid sequences to see which encode a 7 to 100 amino acid piece of the polypeptides set forth as SEQ ID NOs:39 or 44. One of ordinary skill can readily envision fragments as claimed based on the disclosure provided in the specification as filed, thus, Applicants respectfully assert that specification as filed meets the legal requirement for written description under 35 U.S.C. §112, first paragraph. Therefore, Applicants respectfully request withdrawal of the rejection of claim 9, and the claims that depend from this claim including claims 18, 19, and 50 under 35 U.S.C. §112, first paragraph.

Claim 40

The Examiner rejected claim 40 under 35 U.S.C. §112, first paragraph, and suggested at page 4 of the Office Action that the "claims that relate to antisense do not set forth a function." Applicants respectfully disagree with this conclusion. The antisense nucleic acid compositions set forth in claim 40 include antisense nucleic acids that not only bind *in vitro* to a tumor associated nucleic acid, but also must function to reduce the expression of the tumor associated nucleic acid *in vitro*. Thus, the claimed antisense molecules are limited both by sequence and by

function, and contrary to the Examiner's conclusion, there are not an "unlimited number of sequences that meet the broad scope of the claims." (Office Action at page 4).

Applicants respectfully submit that sufficient description is provided in the specification as filed for one of ordinary skill to recognize that Applicants were in possession of the claimed invention at the time of filing. Therefore, Applicants respectfully request withdrawal of the rejection of claim 40 under 35 U.S.C. § 112, first paragraph.

As set forth in the arguments presented above, Applicants respectfully submit that sufficient description is provided in the specification as filed for one of ordinary skill to recognize that Applicants were in possession of the claimed invention at the time of filing. Thus, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1, 9, 18, 19, 40, 50-56, 59, and 60 under 35 U.S.C. § 112, first paragraph.

Rejections Under 35 U.S.C. §112, Second Paragraph

The Examiner rejected claims 1, 9, 18, 19, 43-56, and 58-60 under 35 U.S.C. §112, second paragraph as indefinite. As suggested by the Examiner, Applicants have amended claims 1, 9, 43, and 60 to include sequence identifier numbers for the GenBank Accession numbers disclosed in the specification as filed. Applicants provide herewith copies of the NCBI Sequence publications indicating the date of deposit and any later updates in the published sequences and/or descriptions. The document for each sequence indicates that the sequences provided are the same as those publicly available on the date of filing of the instant application. The sequence of GenBank accession number U89672 (SEQ ID NO:45) was published March 21, 1997 and has not been updated since that date. The sequence of GenBank accession number AA213817 (SEQ ID NO:46) was published December 10, 1996 and was updated Aug 13, 1997. The sequence of GenBank accession number W86797 (SEQ ID NO:47) was published July 1, 1996 and has not been updated since that date. Each of the sequences added to the application is identical to the sequence of its corresponding GenBank accession number that was available on the date of filing of the instant application. Therefore, the amendment of the specification to include the

nucleotide sequences of GenBank accession numbers: U89672, AA213817, and W86797, which are set forth as SEQ ID NOs: 45, 46, and 47 does not introduce new matter into the application.

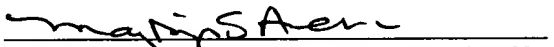
Applicants submit that the inclusion of the Sequence Identification Numbers in the claims obviates the basis of the rejection and therefore respectfully request reconsideration and withdrawal of the rejection of claims 1, 9, 43, and 60 under 35 U.S.C. §112, second paragraph.

CONCLUSION

In view of the foregoing amendments and remarks, this application should now be in condition for allowance. A notice to this effect is respectfully requested. If the Examiner believes, after reviewing the amendments and this response, that the application is not in condition for allowance, the Examiner is requested to call the Applicants' representative at the telephone number listed below.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicants hereby request any necessary extension of time. If there is a fee occasioned by this response, including an extension fee that is not covered by an enclosed check, please charge any deficiency to Deposit Account No: 23/2825.

Respectfully submitted,

By: 

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